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Palladium(II)-mediated cyclization–carbonylation of 4-yn-1-ones: facile access to 2-cyclopentenone carboxylates

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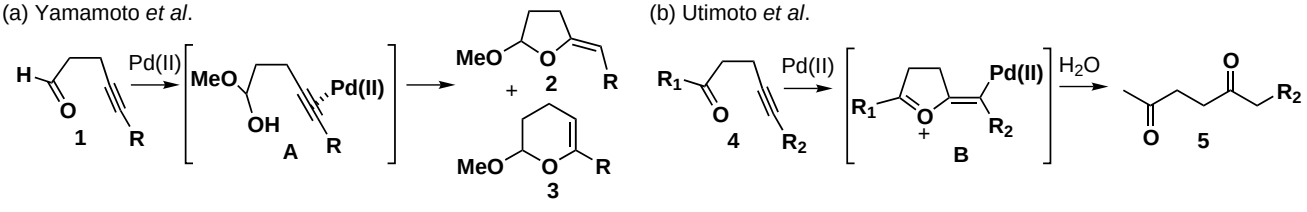
Abstract—The oxidative cyclization–carbonylation of 4-yn-1-ones **6** in the presence of $(CH_3CN)_2PdCl_2$/*p*-benzoquinone in methanol under a carbon monoxide atmosphere (balloon) afforded cyclic-ketals **7** in good to moderate yields. The product **7** were easily converted into 2-cyclopentenone carboxylates **11** and **12**.

Palladium(II)-catalyzed reactions are fundamentally important in organic transformations.[1] Carbonylation of alkynes mediated by palladium is a useful method for the synthesis of acetylene carboxylates,[2] γ-lactones,[3] and benzofurans.[4] Compared with the impressive evolution of palladium(II)-catalyzed carbonylations of alkynyl alcohols,[3–5] that of alkynyl ketones has received only scant attention. Recently, Yamamoto et al.[6] reported a palladium(II)-catalyzed cyclization of alkynyl aldehydes **1** via the hemiacetal intermediate **A** (Scheme 1 (a)). On the other hand, Utimoto et al.[7] reported regioselective hydration of alkynyl ketones **4** controlled by neighboring group participation of the carbonyl group depicted as intermediate **B** in Scheme 1 (b). To the best of our knowledge, previous work on palladium-catalyzed cyclization–carbonylation of γ,δ-unsaturated ketones has been limited to the reaction of alkenyl ketones.[8] Recently, Marshall et al. have reported that Pd(II)/*p*-benzoquinone catalyzed alkoxycarbonylation of δ-alkynyl alcohols to afford methyl pyranosides.[5e] In addition, we have also reported the oxidative cyclization–carbonylation of 4-yn-1-ols using the same catalytic system for the synthesis of (*E*)-cyclic-β-alkoxyacrylates,[5f] its application to the total synthesis of antibiotic natural products,[5g] and the first asymmetric version of this type of reaction.[5h] Now we wish to report here the cyclization–carbonylation of 4-yn-1-ones **6** mediated by palladium(II) and a facile access to 2-cyclopentenone carboxylates (Scheme 2).

The reaction of 5-yn-2-one **6a** bearing a quaternary carbon at the α-position in the presence of $(CH_3CN)_2PdCl_2$[9]/*p*-benzoquinone in methanol at room temperature under a carbon monoxide atmosphere (balloon) afforded cyclic-ketals **7a** in 82% yield as a single diastereomer (entry 1, Table 1).[10] In the case of **6b** and **6c**, the products **7b** and **7c** were obtained as a 3:1 and 1:1 diastereomeric mixture, respectively (entries 2 and 3). The six-membered ring substrates **6d** and **6e** possessing a quaternary carbon at the α-position afforded **7d** and **7e** as a single diastereomer together with methoxy acrylates **8d** and **8e**, respectively (entries 4 and 5). The use of a five-membered ring substrate **6f** and cyclohexanecarboxylate **6g** gave the starting mate-



Scheme 1.

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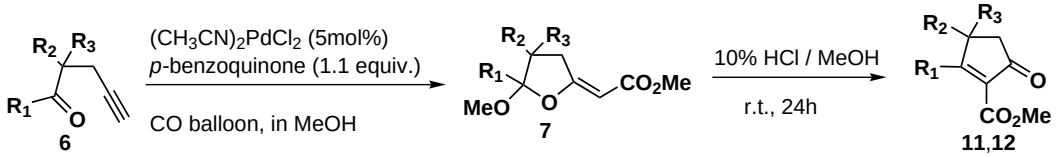
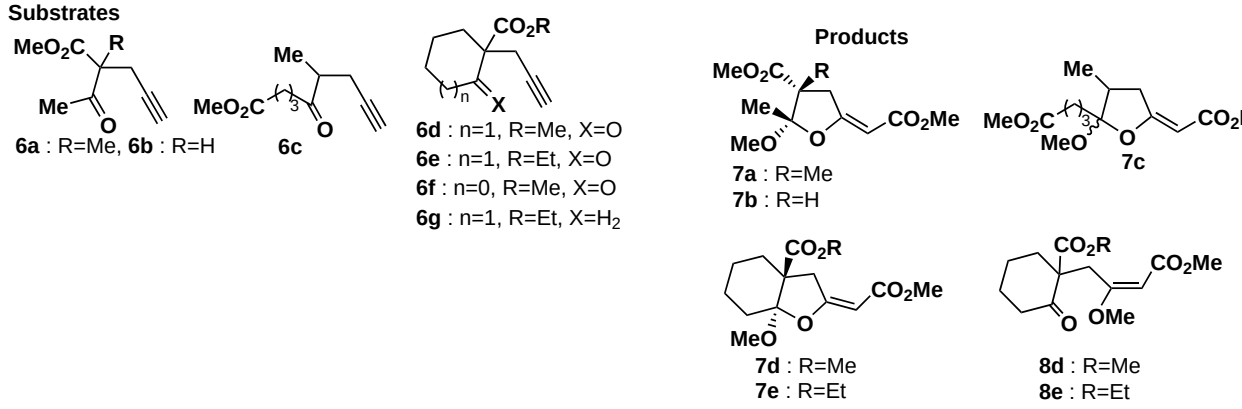


Scheme 2.

Table 1. Cyclization–carbonylation of 4-yn-1-ones **6**

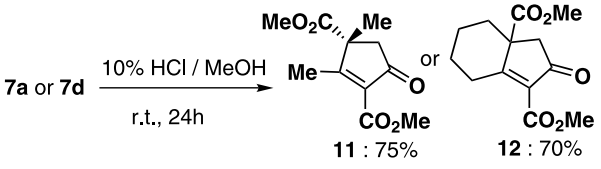


Entry	Substrate	Conditions	Products (yield %)
1	**6a**	0°C–rt, 1 h	**7a** (82)
2	**6b**	0°C–rt, 1 h	**7b** (51)[a]
3	**6c**	0°C–rt, 0.5 h	**7c** (95)[b]
4	**6d**	0°C–rt, 1 h	**7d** (64), **8d** (16)
5	**6e**	0°C–rt, 1 h	**7e** (70), **8d** (20)
6	**6f**	0°C–rt, 7 h	Recovered
7	**6g**	0°C–rt, 3 h	Recovered

[a] The product **7b** was obtained as a 3:1 diastereomeric mixture.
[b] The product **7c** was obtained as a 1:1 diastereomeric mixture.

rials. Acid treatment of the products **7a** and **7d** afforded 2-cyclopentenone carboxylates **11** and **12** in moderate yield (Scheme 3). These reactions presented a facile method for the synthesis of 2-cyclopentenone carboxylates, being a useful intermediate of natural products. The stereochemistry of **7a**, **7d** and **7e** was confirmed by NOE experiment after conversion into diols **9** and **10** by reduction with DIBAL-H as depicted in Fig. 1.

A conceivable mechanism of the present reaction would be proposed as shown in Scheme 4 on the basis of the following experimental results. (1) The reactions of **6f** and **6g** did not proceed as mentioned above, which suggested that the presence of neighboring group participation of the carbonyl group is indispensable for initiating the reaction. (2) In the case of **6a**, **6d** and **6e** bearing a quaternary carbon at the α-position, the products **7a**, **7d** and **7e** were obtained as single diastereomers. These results suggested the formation of a cyclic intermediate **C** (Scheme 4). The coordination of the alkyne to Pd(II) could be induced by attack of carbonyl oxygen to alkyne from the side opposite the palladium to produce the cyclic intermediate **C**. A nucleophilic attack of MeOH on the carbon atom of the cationic carbonyl group from the side opposite the methyl ester group, followed by CO insertion and subsequent reaction with MeOH, provided the acetal products **7d** (path a). On the other hand, the methoxyacrylate **8d** would be produced by the attack of MeOH to the olefinic carbon of vinyl palladium intermediate **C** followed by CO insertion and subsequent reaction with MeOH (path b).[11]



Scheme 3.

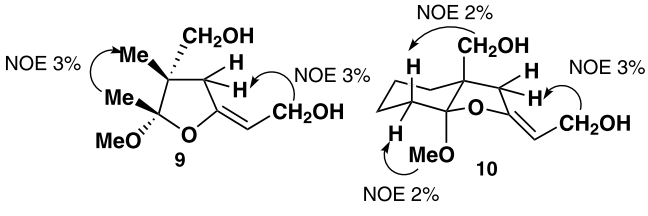
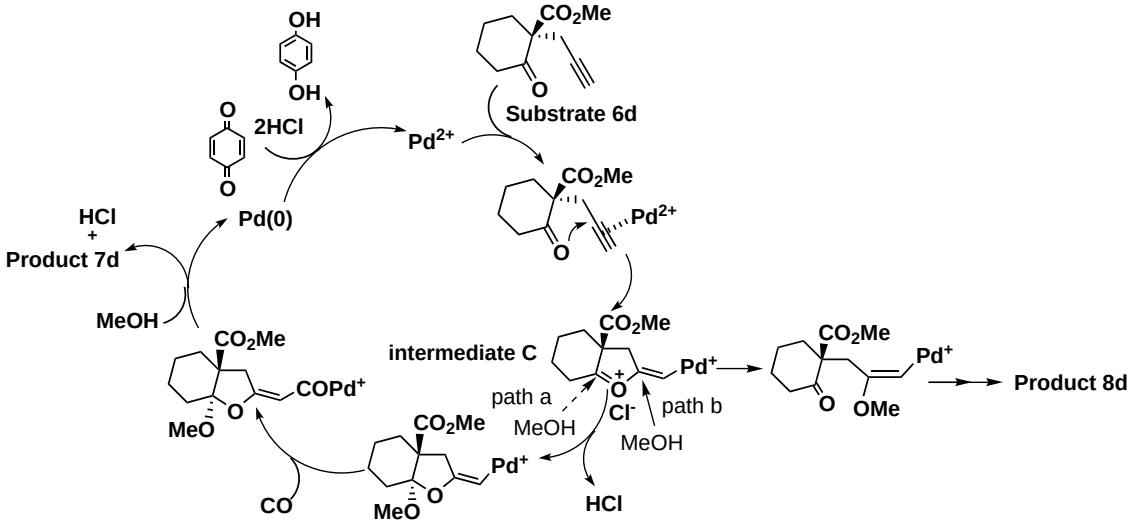


Figure 1.



Scheme 4.

In summary, we have presented new type cyclization–carbonylation of 4-yn-1-ones **6** using a Pd(II)/*p*-benzoquinone catalytic system under mild conditions. The present reaction is considered to be efficient for the synthesis of 2-cyclopentenone carboxylates.

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9. At first, some kinds of palladium catalysts were examined in cyclization–carbonylation of **6a**. Among them, bis(acetonitrile)dichloropalladium(II) gave good results.
10. General procedure: A 30 mL two-necked round-bottomed flask, containing a magnetic stirring bar, $(CH_3CN)_2PdCl_2$ (0.01 mmol), *p*-benzoquinone (0.22 mmol) and MeOH (4 mL) was fitted with a rubber septum and a three-way stopcock connected to a balloon filled with carbon monoxide. The apparatus was purged with carbon monoxide by pumping–filling via the three-way stopcock. A solution of the substrate **6** (0.2 mmol) in MeOH (2 mL) was added dropwise to the stirred mixture via a syringe at 0°C. After being stirred for the period of time, the mixture was diluted with CH_2Cl_2 (30 mL), washed with 5% aq. NaOH (40 mL), and dried over $MgSO_4$. The crude product was purified by column chromatography on silica gel. The fraction eluted with hexane/ethyl acetate (50/1–5/1) afforded **7** and **8** as a colorless oil. Satisfactory analytical data were obtained for all new compounds. Compound **7a**: ^{1}H NMR (400 MHz, CD_3COCD_3): δ 1.24 (3H, s), 1.59 (3H, s), 3.17 (1H, dd, $J=18.0$, 1.2 Hz), 3.24 (3H, s), 3.59 (1H, dd, $J=18.0$, 2.4 Hz), 3.60 (3H, s), 3.68 (3H, s), 5.27 (1H, dd, $J=2.4$, 1.2 Hz); ^{13}C NMR (400 MHz, CD_3COCD_3): δ 15.3, 21.5, 40.6, 50.2, 50.8, 52.4, 55.5, 92.7, 112.7, 168.4, 172.4, 173.3. Compound **11**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.52 (3H, s), 2.31 (3H, s), 2.37 (1H, d, $J=18.6$ Hz), 2.98 (1H, d, $J=18.6$ Hz), 3.73 (3H, s), 3.87 (3H, s); ^{13}C NMR (400 MHz, $CDCl_3$): δ 15.3, 22.2, 47.6, 52.1, 52.4, 53.0, 132.4, 163.3, 173.0, 183.8, 200.2.
11. The products **7d** and **8d** were independently treated with the same reaction condition.[9] No change was observed in both cases and the starting materials **7d** and **8d** were recovered respectively. These results suggested that the product **7d** and **8d** were not produced from **8d** and **7d**, respectively.